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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER				
WILSON, MICHAEL C				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/541,683

Applicant(s)

SCHWENK ET AL.

Examiner

Michael C. Wilson

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-19, 24, 25, 28-30, 32-41, 43-46, 48 and 53-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-19, 24, 25, 28-30, 32-41, 43-46, 48 and 53-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-849)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6-30-09 has been entered.

Claims 1-16, 20-23, 26, 27, 31, 42 have been canceled. Claims 17-19, 24, 25, 28-30, 32-41, 43-56 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's arguments filed 10-6-08 have been fully considered but they are not persuasive.

Election/Restrictions

Claims 47 and 49-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 1-28-08.

Claims 17-19, 24, 25, 28-30, 32-41, 43-46, 48 and 53-56 are under consideration.

Claim Rejections - 35 USC § 101

The rejection of claims 53-56 under 35 U.S.C. 101 has been withdrawn in view of the amendment.

Claim Rejections - 35 USC § 112

New Matter

Claims 53-56 remain and claims 17-19, 24, 25, 28-30, 32-41, 43-46, 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 17 is new matter as amended because the specification does not teach or suggest "wherein the promoter is heterologous to the Rosa26 locus or said functional DNA sequence is a DNA sequence which can be converted into such gene expression cassette." Applicants argue support for the promoter that is "heterologous to the Rosa26 promoter" can be found in claim 31. Applicants' argument is not persuasive. Claim 31 was rejected in the last office action as being new matter. Support for such promoters cannot be found. Furthermore, support for the option of having a promoter that is "heterologous to the Rosa26 locus or said functional DNA sequence is a DNA sequence that can be converted into such gene expression cassette."

The rejection of claim 31 has been withdrawn in view of the amendment.

Claim 53 remains new matter. Support cannot be found for expressing a gene of interest and evaluating the function of the gene. Applicants point to pg 5, line 9-10,

which teaches the transgenic can be used for gene function studies. Applicants' argument is not persuasive. Pg 5 does not teach the steps of expressing a gene of interest and evaluating the function of the gene as claimed.

Claim 54 remains new matter. Support cannot be found for evaluating the effect of the drug on the gene. Applicants point to pg 5, line 9-10, which teaches the transgenic can be used for drug development. Applicants' argument is not persuasive. Pg 5 does not teach the steps of contacting a drug candidate with a biological entity and evaluating the effect of the drug as claimed.

Claim 55 remains new matter. Support cannot be found for providing an animal model of disease, "expression of the gene of interest models a disease state of said animal", contacting a "biological entity" with a drug candidate, and evaluating the effect of the drug on the gene of interest. Applicants point to pg 5, line 9-10, which teaches the transgenic can be used as disease model animals. Applicants' argument is not persuasive. Pg 5 does not teach using models of disease to test drugs or "expression of a gene of interest models a disease state."

Claim 56 remains new matter. Support for step a) is found on pg 9, last 6 lines. Support for step c) is found on pg 10, lines 1-2. Support for step b) cannot be found. Applicants point to the paragraph bridging pg 9-10. The paragraph discusses steps a) and c) of claim 56 but not step b).

Indefiniteness

Claims 17-19, 24, 25, 28-30, 32-41, 43-46, 48 and 53-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection regarding claim 17 regarding "mammalian eukaryotic" has been withdrawn in view of the amendment.

The rejection of claim 18 has been withdrawn in view of the amendment.

Claim 17 is newly rejected as being indefinite amended because the "modified Rosa26 locus" is unclear and does not clearly set for the structure of the Rosa26 nucleic acid sequence or Rosa26 gene. The structure modified is a Rosa26 gene, not the "position" or "locus" of the Rosa26 gene. Replacing "locus" with --gene-- is required.

Claim 19 remains indefinite because the phrase "site specific recombinase mediated recombination" is unclear. The metes and bounds of the phrase are not defined in the specification or the art at the time of filing. Therefore, those of skill would not know when they had performed that type of site specific recombination. Applicants argue the technique was well known in the art and cite pg 9-10. Applicants' argument is not persuasive. Applicants' argument is unfounded. Furthermore, the art did not define when recombination was "specific" to a site or how close recombination must be to be "specific."

Claim 28 remains indefinite because the metes and bounds of what applicants consider "primary" cannot be determined. The term is not defined in the specification or the art at the time of filing. Applicants argue the term was used in the art at the time of filing. Applicants' argument is not persuasive. Applicants' argument is unfounded.

Furthermore, the art at the time of filing did not define "primary" cells. Without a definition, those of skill would not know when they were infringing on the claim.

Claim 30 remains indefinite because the phrase "pharmaceutically active proteins and peptides" is unclear. It is unclear when a protein or peptide is pharmaceutically active as claimed. Applicants argue the phrase "pharmaceutically active" was used in the art at the time of filing. Applicants' argument is not persuasive. Applicants' argument is unfounded. Furthermore, the art at the time of filing did not define when proteins and peptides are "pharmaceutically active" as claimed. Without a definition, those of skill would not know when they were infringing on the claim.

The rejection of claim 31 has been withdrawn because the claim has been canceled.

The metes and bounds of what applicants consider an "inducible ubiquitous promoter" and "inducible tissue specific promoter" in claim 32 cannot be determined. The structure of such promoters is not defined in the specification or the art at the time of filing. Applicants argue the phrases are well known promoter genera and species. Applicants point to the first paragraph on pg 8. Applicants' argument is not persuasive. Applicants' argument regarding the art at the time of filing is unfounded. Furthermore, the art at the time of filing did not define which promoters are "inducible ubiquitous promoters" and "inducible tissue specific promoters". Without a definition, those of skill would not know when they were infringing on the claim.

The metes and bounds of what applicants consider a "CAGGS, hCMV, PGK, FABP, Lck, CamKII, CD19... ..aP2... ..MCK, MyHC, WAP, Col2A, Mx, tet and trex"

promoter in claim 33 cannot be determined. The structure of such promoters is not defined in the specification or the art at the time of filing. Applicants argue the phrases are well known promoter genera and species. Applicants point to the first paragraph on pg 8. Applicants' argument is not persuasive. Applicants' argument regarding the art at the time of filing is unfounded. Furthermore, the art does not teach what the abbreviations stand for. The abbreviations should be spelled out where necessary or applicants should point to the definition of such abbreviations in the specification or the art at the time of filing.

The rejection of claim 34 has been withdrawn in view of the amendment.

Claim 35 is indefinite because the phrase "the targeting vector or recombination vector" lacks antecedent basis in claims 18 and 19. The phrase "the targeting vector" lacks antecedent basis in claim 19 and the phrase "the recombination vector" lacks antecedent basis in claim 18. Applicants' arguments have been considered but are not persuasive. The phrases apply to only one claim and not both claims 18 and 19 as claimed. The "targeting vector" should clearly refer to claim 18 and the recombination vector should clearly refer to claim 19.

The rejections of claim 38 have been withdrawn in view of the amendment.

The rejection of claim 40 has been withdrawn in view of the amendment.

The rejection of claim 41 has been withdrawn in view of the amendment.

Claim 45 remains indefinite because it is unclear what applicants consider an "inactive" positive selection marker. Applicants argue the markers were known to those of skill in the art at the time of filing. Applicants' argument is not persuasive. Applicants'

argument regarding the art at the time of filing is unfounded. The phrase was not defined by applicants or those of skill in the art at the time of filing. Therefore, those of skill would not know when they were infringing on the claim.

Claim 46 remains indefinite as amended it appears there are three steps, but only steps a) and b) are specified. Furthermore, it is unclear how the step of "isolating the transgenic non-human mammalian cells" differs from "isolating the transgenic non-human mammalian cells having a modified functional DNA sequence." The phrase "isolating the transgenic non-human mammalian cells having a modified functional DNA sequence" is redundant and should be deleted. Applicants indicate they are not sure why the examiner thinks there are three steps. There are three steps because there are three active steps: "isolating," "modifying" and "isolating." If the second "isolating" step is intended to mean modified functional DNA obtained from step b) isolated, such a step should be clearly set forth, i.e. "isolating the modified functional DNA sequence obtained from step b)."

Claim 48 remains indefinite. Claim 48 is a non-human mammalian cell obtained from the method of claim 17; however, it cannot be determined how the process of claim 17 further limits the structure "non-human mammalian cell having a modified Rosa26 locus" as in claim 48. The structure of the cell in claim 48 is not clear from the method of claim 17. Also, a cell can have a genetically altered Rosa26 gene, but a cell does not have a modified Rosa26 "position" or "locus". Applicants do not substantially address this rejection or indicate the structure or function of the cells in claim 48.

Claims 53-55 remain indefinite as amended because they require providing a eukaryotic cell, a transgenic multi-cell non-human organism or a transgenic non-human mammal using the method of claim 17; however, claim 17 is limited to making a transgenic non-human mammalian cell. Applicants do not address this rejection.

Claims 53-55 are newly rejected as being indefinite because the claims require a cell, organism or mammal "obtainable utilizing the method of claim 17" but do not clearly set forth the cell, organism or mammal are obtained by the method of claim 17.

The rejection of claims 53-55 regarding "the gene of interest" has been withdrawn.

Claims 54 and 55 remain indefinite because they do not set forth any steps for "drug development." Evaluating the effect of the drug candidate on a gene of interest (claim 54) or expression of a gene of interest (claim 55) does not result in drug development as claimed. Applicants argue the amendment clarifies the claim. Applicants' argument is not persuasive.

Claim 55 remain indefinite because it is unclear how an animal comprising a non-human mammalian cell made by the method of claim 17 is a model of an animal disease. Applicants argue even a cell can be used to test drugs. Applicants' argument is not persuasive because a cell is not a model of disease.

Claim 56 remains indefinite because the metes and bounds of what applicants consider "two mutually incompatible RRSs" does not clearly set forth the structure or function of the acceptor DNA. Clarification is required. Applicants argue examples of such RRSs are provided in the specification. Applicants' assertion is unfounded.

The rejection of claim 56 regarding "recombination vector" and the "functional DNA sequence" in step b) has been withdrawn in view of the amendment.

The rejection of claim 56 regarding the recombinase in step c) has been withdrawn.

Claim Rejections - 35 USC § 102

Claims 17-25, 28-30, 32-32, 34-38, 43-46, 48 and 53-56 remain rejected under 35 U.S.C. 102(b) as being anticipated by Soprano (WO99/53017) for reasons of record.

Soriano made a Rosa26 transgenic mouse by introducing a DNA cassette comprising a LacZ gene flanked by loxP sites into the Rosa26 locus of a mouse ES cell and implanting the ES cell into a mouse blastocyst. The LacZ gene was under the control of the mouse Rosa26 promoter (Example 1, pg 30). Soriano also taught making a Rosa26Cre transgenic mouse (Example 2, pg 41) by introducing a construct into ES cells, the construct comprising a deleter cassette comprising a recombinase gene operably linked to an upstream splice acceptor (SA and a downstream polyA sequence with a positive selection cassette comprising a PGK promoter, the neo gene and a polyadenylation sequence (pg 7, lines 2-10). The construct was inserted into the targeting vector comprising homology arms for the Rosa26 gene and a diphtheria toxin gene for negative selection (pg 7, line 9-10; pg 7, line 1-2). Soriano also made a transgenic mouse by introducing a targeting vector into mouse ES cells, the vector comprising a reporter cassette comprising a splice acceptor operably linked to stuffer DNA flanked by two loxP sites (pg 7, lines 10-16); the stuffer DNA comprised a PGK promoter, the neo gene and four polyA sites (pg 44, Example 3). The coding sequence

described by Soriano is a "DNA sequence which can be converted into such gene expression cassette." The claim is not limited to a promoter that is heterologous to the Rosa26 locus because the claim as amended indicates such a promoter is optional ("wherein said promoter is heterologous to the Rosa26 locus or said functional DNA sequence is..."). In the alternative, Soriano taught numerous Rosa26 promoters which are "heterologous" as claimed because they are non-naturally occurring promoters.

Applicants argue Soriano did not teach the promoter was heterologous to the ROsa26 locus. Applicants' argument is not persuasive. The claim is not limited to a promoter that is heterologous to the Rosa26 locus because the claim as amended indicates such a promoter is optional ("wherein said promoter is heterologous to the Rosa26 locus or said functional DNA sequence is..."). In the alternative, Soriano taught numerous Rosa26 promoters which are "heterologous to the Rosa26 locus" as claimed because they are non-naturally occurring promoters.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Patent Examiner